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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,360	02/26/2007	Arkady Mandel	355908-3451	5554

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,360	MANDEL ET AL.	
	Examiner	Art Unit	
	GOLLAMUDI S. KISHORE	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7-24-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims included in the prosecution are 1-15.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 28-32, 58-61 and 74-88 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the in vitro effectiveness of phosphatidylglycerol in inhibiting the secretion of TNF alpha from the macrophages, does not reasonably provide enablement for phosphate containing groups or phosphate glycerol groups or groups convertible to such groups and the prevention or treatment of acute inflammatory disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d, 1400 (Fed.Cir.1988). Among these factors are: (1) the nature of the invention; 2) the state of the prior art; 3) the relative skill of those in the art; 4) the predictability or unpredictability of the art; 5) the breadth of the claims; 6) the amount of direction or guidance presented; 7) the presence or absence of working examples; and 8) the quantity of experimentation necessary. When the above factors are weighed, it is

the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

1) The nature of the invention: the invention is concerned with treating an acute inflammatory comprising the administration to a mammalian subject an effective amount of bodies comprising an effective number of phosphate-glycerol groups or phosphate containing groups or groups convertible to such groups.

2) The state of the prior art: the state of the prior art is very high in terms of formulating the liposomal sustained release compositions and treating various disease states using drugs which are encapsulated within the liposomes. However, phospholipids as such which occur naturally within mammalian bodies are not known as effective in the treatment of any disease except that some phospholipids such as lecithin are known for the removal of cholesterol from the blood. Even lecithin is not known for their routine use as an anti-cholesterol drug.

3) The relative skill of those in the art: the skill of one of ordinary skill in the art is very high (Ph.D level technology).

4) The predictability or unpredictability in the art: There is no evidence in literature of the phosphate containing groups (nucleosides for example) or phosphate-glycerol containing groups or groups convertible to these groups are able to treat inflammatory disorders

5) The breadth of the claims: instant claims are very broad in terms of bodies containing phosphate-glycerol groups and phosphate containing groups and groups convertible to such groups.

6) The amount of direction of guidance provided: instant specification provides no guidance to the treatment of a patient suffering from claimed diseases, some of which are hereditary diseases using the phosphate-glycerol groups. Just because there is an inappropriate cytokine expression in the claimed diseases and phosphatidylglycerol has some effect on the cytokines, one cannot predict the effectiveness of the compound in the treatment of disease itself. It is understandable if the cytokine expression is the causative factor for the disease and applicant has not established that the cytokine expression is responsible for expression of various disease states. The specification contains some in vitro studies on cytokines and nothing else. In contains no data as to how the claimed bodies containing phosphate-glycerol groups are effective in the treatment of various diseases.

7) The presence or absence of working examples: the only working examples provided are not even connected with the diseases claimed in instant claims. In the working example, Applicant shows the effectiveness of phosphatidylglycerol on the inhibition of the secretion of TNF alpha into the surrounding medium from the macrophages and nothing else. Furthermore, instant claims are drawn to both prevention and treatment of the acute inflammatory disorder and applicant has not presented any data to show that the condition can be prevented by the administration of claimed bodies.

8) The quantity of experimentation necessary: It would require undue experimentation to determine the effectiveness of phosphatidylglycerol in the treatment of various diseases claimed.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear as to what applicant conveys by the terms such as 'bodies', 'phosphate containing groups', 'phosphate-glycerol groups and 'groups convertible to such groups' in claim 1. Taking phosphatidylglycerol for example, it has fatty acid chains on C1 and C2 of the glycerol moiety and they have the ability to form liposomes.

"entities other than phosphate-containing surface groups' in claim 7 is not a positive recitation and therefore, renders claim 7 indefinite.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1-10 and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Onyuksel (US 2002/0115609).

Onyuksel discloses a method of treatment of inflammation (arthritis) using micellar compositions containing phosphatidylglycerol (0036, 0052, 0053, 0071, 0075, 0082, 0147 and claims). Instant claims are drawn to a treatment of acute inflammatory condition. Since prior art teaches inflammatory conditions; instant claimed down

regulation of one anti-inflammatory cytokine and up regulation of one pro-inflammatory cytokine are inherent function of the phosphatidylglycerol.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-10 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Jorgensen (US 2002/0001614) of record.

Jorgensen discloses liposomal compositions containing phospholipids for the treatment of inflammatory conditions (abstract, 0056, 0066, 0080, 0017-0129). Since prior art teaches inflammatory conditions; instant claimed down regulation of one anti-inflammatory cytokine and up regulation of one pro-inflammatory cytokine are inherent function of the phosphatidylglycerol. The reference meets the requirements of instant claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berger Am J Respir Crit Care Med (1999).

Berger teaches that dioleylphosphatidylglycerol modulates the inflammatory reaction and it down regulates the expression of sPLA2-II through the inhibition of TNF-alpha secretion (column 2, page 613). Berger uses liposomes containing either DPPG alone or in combination with DPPC (col. 1, page 614, Figure 5). Therefore, it would have been obvious to one of ordinary skill in the art to administer liposomes containing phosphatidylglycerol to treat acute inflammatory conditions based on the suggestion of Berger with a reasonable expectation of success. Although Berger does not specifically teach the sizes of the liposomes, instant claims recite a broad range of 20 nm to 500 micrometers. Since Berger teaches sonication followed by filtration through 0.45 micrometer filters, it would have been obvious to one of ordinary skill in the art that the diameters will be less than 0.45 microns.

10. Claims 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Onyuksel or Jorgensen cited above.

The teachings of Onyuksel and Jorgensen have been discussed above. Although the references teach 'inflammation' in general, they do not teach the claimed specific inflammatory conditions. However, since the compositions of Onyuksel and Jorgensen are for the treatment of inflammation, it would have been obvious to one of ordinary skill in the art that the composition can be used to treat any inflammatory condition with a reasonable expectation of success.

The references of Fogelman, Wendel and Lefer which teach the use of phospholipids for treating inflammation are cited as interest.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GOLLAMUDI S. KISHORE whose telephone number is (571)272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore/
Primary Examiner, Art Unit 1612

GSK